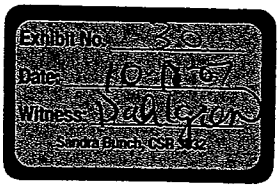
TOXICOLOGICAL REVIEW AND CRITERIA FOR EVALUATION OF EXPOSURE TO METHYL *TERT*-BUTYL ETHER IN DRINKING WATER

August 2000



New York State Department of Health
Center for Environmental Health
Bureau of Toxic Substance Assessment

Flanigan Square, 547 River Street
Troy, New York 12180-2216

PREFACE

The Bureau of Toxic Substance Assessment of the New York State Department of Health prepared this criteria document to assist in evaluating the health risks of exposure to methyl *tert*-butyl ether (MTBE) in drinking water. This document is not intended to be an exhaustive review of the MTBE literature, but is focused upon those data thought to be most relevant to human health risk assessment. The scientific literature was reviewed (last literature search update August 2000) and key studies evaluated to provide a qualitative and, to the extent possible, quantitative assessment of the toxicity of MTBE.

The criteria characterize the human health risks associated with exposure to MTBE in drinking water. The quantitative criteria developed in this document are not, in themselves, rules, or standards. They are based solely on data and scientific judgments on the relationship between MTBE drinking water and health risks, and do not reflect consideration of other factors, such as economic analysis and technological feasibility, which are evaluated when establishing regulatory requirements for drinking water contaminants.

Toxicological Assessment Section
Bureau of Toxic Substance Assessment
New York State Department of Health

EXECUTIVE SUMMARY

Methyl *tert*-butyl ether (also called MTBE) is a colorless, synthetic liquid with an unpleasant taste and odor. MTBE is a gasoline additive used in the United States, including New York State, to reduce air pollution from gasoline engines. MTBE is a small, highly soluble molecule and does not bind strongly to soils. Gasoline spills and leaking gasoline storage tanks have contaminated groundwater with MTBE because MTBE travels rapidly to and through surface water and groundwater. The potential health effects of MTBE are of concern because many communities rely upon groundwater for their drinking water. This document reviews the current scientific literature on MTBE and derives criteria based on the potential for non-cancer and cancer health risks to humans exposed to MTBE in drinking water.

Studies on the human health effects of oral MTBE exposures were not found. Thus, the identification and evaluation of the potential human health effects from long-term exposure to MTBE in drinking water are based on the results of animal studies. The limited data on the pharmacokinetics of MTBE in humans and animals support this approach.

Animal data show that the targets for MTBE toxicity are the central nervous system, gastrointestinal tract, kidney, liver, and blood, and that MTBE can cause developmental effects at doses that also harm the pregnant adult animal. The animal data do not indicate that MTBE can cause reproductive effects. Based upon a review of the strengths and limitations of oral studies and selected inhalation studies for estimating potential human non-cancer risks from low-level oral doses of MTBE, the dose-response data from a subchronic study of systemic toxicity (diarrhea and blood chemistry changes) in rats are used to derive an adult drinking-water criterion of 200 micrograms per liter (ug/L) for non-cancer effects. The derived drinking-water criterion is protective of effects in children and of developmental effects observed in the offspring of female animals exposed to MTBE in air during pregnancy or before, during, and after pregnancy.

Given the available data, 200 ug/L is an estimate of the highest MTBE level in drinking water that is not likely to pose an appreciable non-cancer risk to chronically-exposed populations, including sensitive groups. The criterion is not an exact boundary between water levels that are safe and those that are not. For most people, exposure to water levels above, but near the criterion, will not cause non-cancer effects. However, the possibility exists, although unlikely,

that some people exposed to levels slightly below the criterion will show non-cancer effects. This uncertainty is unavoidable because inferring risks at dose levels substantially below the lowest daily dose associated with observable effects in animal studies is an uncertain process and our knowledge of the toxicological effects of oral doses is limited.

Various federal and state agencies have identified MTBE as an animal carcinogen. Oral and inhaled doses of MTBE caused cancer in laboratory animals. MTBE induced lymphomas/leukemias in female rats after gavage doses, testicular tumors (Leydig cell adenomas) in male rats after gavage doses or inhalation exposures, kidney tumors in male rats after inhalation exposures, and liver tumors in male and female mice after inhalation exposures. Based upon a review of the strengths and limitations of each data-set for estimating potential human cancer risks from low-level oral doses of MTBE, a quantitative estimate of the human cancer potency of MTBE in drinking water is based on dose-response data for testicular tumors (Leydig cell adenomas) in male rats given gavage doses of MTBE. The derived cancer potency factor is 3.2×10^{3} per milligram per kilogram body weight per day. This leads to a drinking-water criterion of 10 ug/L for cancer effects, which is the water concentration corresponding to the lower-bound estimate on the dose associated with an excess lifetime human cancer risk of one-in-one million. Drinking-water levels associated with excess lifetime human cancer risks of one-in-one-hundred-thousand and one-in-ten-thousand are 100 ug/L and 1,000 ug/L, respectively. Cancer potency factors based on the lymphoma/leukemia data or the inhalation studies are supportive of the selected potency factor, however, they may have greater uncertainty than the selected factor when used to assess the human cancer risk from low-level oral exposures to MTBE.

Because of the uncertainties associated with the animal-based cancer potency estimates, they cannot be used in an actuarial sense to predict the number of actual cancer cases in humans exposed to MTBE in drinking water. The exact degree of risk at low water levels may never be known because the risk is generally too small or too confounded by other factors to measure in the general population, particularly given the large background rate of cancer (lifetime risks of about 33%, or 333,000 per one million women, and 50% or 500,000 per one million men) in the general population.